Schering-Plough
HealthCare Products

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Dockets Management Branch
Food and Drug Administration (HFA-305)
5630 Fishers Lane
Room 1061
Rockville, MD 20857

Comments on Submission CP-11, Docket 78N-0038: Request for Administrative Stay and Citizen Petition for a Comprehensive Final Monograph

Dear Sir or Madam:

Schering-Plough HealthCare Products (SPHCP), a major manufacturer and distributor of sunscreen products in the United States, has been a leader in suncare research for many years. As a member of the joint Consumer Healthcare Products Association/ Cosmetic, Toiletry and Fragrance Association (CTFA) Sunscreen Taskforce, we are aware of the Request for Administrative Stay of Action and Citizen Petition Requesting a Comprehensive Sunscreen Monograph (CP-11) submitted to the Docket by CTFA, dated April 15, 1999. While we fully agree with the purpose of the letter and support the CTFA position that a comprehensive monograph is important and desirable, we feel that it is useful to clarify certain scientific points raised in the subject letter.

In that spirit, we offer the following points of clarification:

1. CTFA Comments, Page 4: "recent medical evidence has made it clear that UVA protection may be the most important factor in preventing skin cancer caused by the sun".

SPHCP Clarification: A review of the medical and scientific literature leads us to the conclusion that, while UVA likely contributes to skin cancer, the primary causative wavelengths are in the UVB range. Other than the very controversial publication by Setlow which studied the development of

melanotic lesions in fish genetically predisposed to pigmented tumors (1), the preponderance of data support the fact that UVB radiation is predominantly responsible for the majority of skin cancers and precancerous lesions (2-5), followed by the shorter UVA waveband (UVA II, 320-340 nm) (6).

Recent investigations into the etiology of p53 mutations and of melanotic lesions have shown that UVA has little if any role in producing either of these key mutations which are precursors to skin cancer development (7, 8). We conclude that the role of UVB in inducing skin cancer and its precursors has been convincingly shown in both human and animal models.

2. *CTFA Comments, Page 6:* "recent scientific findings have confirmed that exposure to UVA radiation is linked to the alarming incidence of serious skin cancer in the United States".

SPHCP Clarification: As noted above and included in the cited published references, the scientific and medical literature attributes the primary cause of ultraviolet-induced skin cancers to the UVB wavelength range.

3. *CTFA Comments, Page 21:* "products that are designed to comply with the Partial Final Monograph will not protect consumers against UVA radiation and will mislead consumers to believe they are protected."

SPHCP Clarification: We are certain that the CTFA letter did not intend to imply that currently marketed sunscreen products fail to provide substantial protection within the UVA wavelength range, especially those with SPF values of 12 or greater and that conform to the testing methods of the Proposed or Tentative Final Sunscreen Monograph. It should be emphasized that the UVA wavelengths contribute significantly to erythema. It has been reported that approximately 20% of the sun's erythemal energy in the summer is from UVA (9). In fact, due to the erythemogenic potency of the shorter UVA wavelengths (i.e., 320 to 340 nm), an SPF value of 12 or greater can not be attained without including some level of UVA absorbance. The Agency has previously set forth labeling guidelines for the inclusion of UVA claims based on the use of UVA-absorbing ingredients (e.g., oxybenzone, dioxybenzone, sulisobenzone, menthyl anthranilate, avobenzone, or zinc oxide).

Schering-Plough HealthCare Products recently provided the Agency with summary data demonstrating that UVA protection generally increases with increasing SPF (Docket Submission C551, January 4, 1999), even for products which do not include longwave UVA (i.e., UVA I, 340-400 nm) absorbers (i.e., avobenzone or zinc oxide).

Perhaps it is not clear in the CTFA letter that the primary issue is more one of finalizing methods to first evaluate and then to describe through labeling the total expected product effectiveness to consumers. The lack of a standardized UVA test method at this time does not mean that currently marketed products do not provide UVA protection.

4. CTFA Comments, Page 22: "the use of sunscreens that protect against UVB radiation but not UVA radiation will confuse the public about the protective efficacy of sunscreen products....." "the use of sunscreens that protect against exposure to UVB radiation but not to UVA will encourage consumers and their children to remain in the sun for longer periods of time, increasing exposure to harmful UVA radiation".

SPHCP Clarification: Many currently marketed sunscreen products provide significant UVA and UVB protection when used as directed. This is especially true of higher SPF products as well as those containing avobenzone and appropriate levels of zinc oxide. These products are extremely important in an overall "safe sun strategy", which includes sun avoidance at peak hours, seeking shade and wearing appropriate clothing, hats and eye protection. Sunscreens are designed to provide protection against ultraviolet damage for the consumer while in the sun, not to encourage them to stay out longer than they had intended. Our longstanding experience with sunscreen products indicates that consumers do understand sunscreen labels and successfully rely on the protection these products afford. Again, we are certain that the CTFA did not intend to imply that currently available sunscreen products do not provide effective protection or that consumers are not able to understand the appropriate use of such products.

In summary, we want to ensure that the wording of the letter provided by CTFA does not leave the mistaken impression that UVA is the primary cause of skin cancer or that currently marketed sunscreen products do not provide significant levels of UVA protection as well as UVB protection, and as such, could mislead the consumer. We concur with CTFA that it is important and beneficial to reach consensus both on a method for evaluating UVA protection and on suitable ways to provide that information to consumers as part of the product labeling.

Sincerely,

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References

1. Setlow RB, Grist E, Thompson K, Woodhead AD. Wavelengths effective in induction of malignant melanoma (platyfish swordtail hybrid). Proc Natl Acad Sci USA 1993;90;6666-6670.

2. Kligman LH, Akin F, Kligman AM. Sunscreens prevent ultraviolet photo-carcinogenesis. J Am Acad Dermatol 1980;3;30-35.

3. Kligman LH, Akin F, Kligman AM. The contributions of UVA and UVB to connective tissue damage in the hairless mouse. J Invest Dermatol 1985;84;272-276.

4. Thompson SC, Jolley D, Marks R. Reduction of solar keratoses by regular sunscreen use. New Eng. J. Med. 1993;329;1147-1151.

5. Naylor MF, Boyd AS, Smith DW, Cameron GS, Hubbard D, Nelder KH. High sun protection factor sunscreens in the suppression of actinic neoplasia. Arch Dermatol 1995;131;170-175.

6. Kelfkens G, deGruijl FR, van der Leun JC. Tumorigenesis by short-wave ultraviolet A. Carcinogenesis 1991;12;1377-1382.

7. Ananthaswamy HN, Fourtanier A, Evans RL, Tison S, Medaisko C, Ulrich SE, Kripke ML. P53 mutations in hairless mouse skin tumors induced by a solar simulator. Photochem Photobiol 1998;67;227-232.

8. Atillasoy E, Seykora J, Soballe P. Elenltsas R, Nesbit M, et al. UVB induces atypical melanocytic lesions and melanoma in human skin. Am J Pathol 1998;152;642-649.

9. Urbach F. Ultraviolet transmission by modern sunscreens: is there a real risk? Photodermatol. Photoimmunol. Photomed. 1993;9;237-241.

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